Sharples Chemicals Inc.

(P.Dev.-1)
(R.Lab.-1)
(Phila- 2)
(W. Copy-1)
(T.Deger-1)
(L.A.G.-1)
(C.W.L.-1)

SUBJECT: TETRAMETHYLTHIURAM DISULFIDE

PART MATERIALS, PHYSIOLOGICAL PROPERTIES

SECTION TOXICITY AND TOXICOLOGY OF TETRAMETHYLTHIURAM DISULPHIDE

We present in the following pages our final report on toxicity and toxicology of tetramethylthiuram disulphide, samples of which have been sent to us by the Wyandotte plant.

1. LD 50 (rabbit, oral administration) = 0.21 gm /kg.

2. Skin effect

   A. The primary irritation of the undamaged skin of rabbits (abdomen) is moderate.

   B. Only 9 per cent of our skin patch tests (dry powder, male students) were slightly positive. However, literature reports and the experiences in the Wyandotte plant do not leave any doubt that the product is a skin irritant which may cause dermatitis of different degree.

3. Effect on lower respiratory tract

   A. Exposure of rabbits to air concentrations not exceeding 0.00127 mg./l., for 33 and 30 consecutive days, 24 hours a day, has led to a marked irritation of the lung tissue.

   B. In the final experiment, rabbits were exposed to a concentration of 0.0019 ± 0.0003 mg./l. for 5 weeks, 5 days a week, 7 hours a day. The majority of the dust particles measured 2 μ and less. The lungs of these animals, too, showed definite signs of irritation (hyperemia, moderate infiltration and occasional pneumonitis).

   In all three experiments, deposits of fine, refractile

particles were found in the lung tissue.

C. Effects on the lungs by feeding the product to rabbits have been suggested but not proven by our experiments.

4. Systemic effects

A. Repeated feeding of large doses (1/2 and 1/4 of the LD 50) led to marked degenerative changes in liver and kidney, and to a decrease in the number of white blood cells.

B. Absorption of the inhaled material has been proven not only by the effects on different organs described below but also by the uniform presence of very fine particles (smaller than 1 μ) in liver, spleen and bone marrow. We have not been able to identify these particles histo-chemically as tetramethylthiuram disulphide, but have no doubt that they are.

Intensive inhalation as described under 3 A (24 hours a day for 33 and 30 days, respectively) produced marked degeneration of liver and kidney tissue similar to that observed in feeding experiments; also reduction of the number of white cells. Fine particle inclusions were found in the tissues.

Milder exposure -- 3 B -- resembling industrial exposure (7 hours a day for 5 weeks, 5 days a week) resulted in a moderate loss of weight but no other uniform changes in the living animal. Autopsy showed congestion of the lungs. The histologic examination revealed marked degenerative changes in liver and kidney, though somewhat less advanced than in the previously mentioned experiments. The lungs showed

congestion and beginning or moderate inflammation (pneumonitis). The bone marrow of the sternum contained more fat than seen in normal rabbits.

Liver, spleen and bone marrow contained moderate to large deposits of fine refractile particles which were definitely not pigment found normally in rabbits.

The foregoing findings allow the following conclusions:

1. Tetramethylthiuram disulphide is a primary skin irritant.
2. Tetramethylthiuram disulphide irritates the lower respiratory tract.
3. Tetramethylthiuram disulphide acts as a systemic poison in producing degenerative changes in several organs. It is absorbed by ingestion and by inhalation.

The following protective procedures are recommended:

1. Hands and arms of people handling the material should be protected.
2. Ingestion and inhalation should be avoided by:
   A. Eliminating or greatly reducing air contamination in the plant. We are not yet in a position to recommend a maximum allowable concentration. However, the air concentrations used in our experiments which had marked toxic effects were only slightly higher than the air concentration found in the immediate vicinity of the pulveriser in the Wyandotte plant (0.0014 mg./l.; May 1946).
   B. Warning labels should be attached to containers.

H. Brieger, M. D.

CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Data produced 8 (Month) 2 (Day) 88 (Year) Barbara Smith Camera Operator

Place Syracuse (City) New York (State)

AMTEK corp